APPENDIX A

74. A pharmaceutical composition for treating a disorder in which TNFα activity is detrimental comprising an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less, and at least one additional therapeutic agent.

75. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNFα with a K_{off} rate constant of 5 x 10^{-4} s^{-1} or less.

76. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-4} s^{-1} or less.

77. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-8} M or less.

78. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-9} M or less.

79. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-10} M or less.

80. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, is a recombinant antibody, or antigen-binding portion thereof.

81. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, inhibits human TNFα-induced expression of ELAM-1 on human umbilical vein endothelial cells.

82. The pharmaceutical composition of claim 74, wherein the isolated human antibody, or antigen-binding portion thereof, is D2E7.

83. The pharmaceutical composition of claim 74, wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-57111/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, thalidomide-related drugs, leflunomide, tranexamic acid, T-614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered peptides, collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immune globulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth

factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, lignocaine, prednisolone, methylprednisolone, cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of cytokines such as TNFα, IL-1β, IL-6 and/or IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, including diethylenetriamine pentaacetic acid - iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy and anti-IL-8 antibodies.

84. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less, and

85. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance,

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO:

3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

86. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent such that human TNFα activity is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

87. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the human subject an antibody and at least one additional therapeutic agent such that human TNFα activity is inhibited, wherein the antibody is D2E7.

88. The method of any one of claims 84, 85, 86, or 87, wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, thalidomide-related drugs, leflunomide, tranexamic acid, T614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin,

anti-CD4 antibodies, CD5-toxins, orally-administered peptides, collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immune globulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, lignocaine, prednisolone, methylprednisolone, cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of cytokines such as TNFα, IL-1β, IL-6 and/or IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, including diethylenetriamine pentaacetic acid - iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy and anti-IL-8 antibodies.

89. The method of any one of claims 84, 85, 86, or 87, wherein the disorder is rheumatoid arthritis.

90. The method of claim 89, wherein the wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, thalidomide-related drugs, leflunomide, tranexamic acid, T614,

prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered peptides, collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immune globulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, and azaribine.

91. The method of any one of claims 84, 85, 86, or 87, wherein the disorder is inflammatory bowel disease.

92. The method of claim 91, wherein the additional therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine.

93. The method of any one of claims 84, 85, 86, or 87, wherein the disorder is multiple sclerosis.

94. The method of claim 93, wherein the additional therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon-β1a,

interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG, 55 kdTNFR-IgG, IL-10, IL-4, and IL-10 agonists, and IL-4 agonists.

95. The method of any one of claims 84, 85, 86, or 87, wherein the disorder is sepsis.

96. The method of claim 95, wherein the additional therapeutic agent is selected from the group consisting of hypertonic saline solutions, antibiotics, intravenous gamma globulin, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6, antagonists of IL-8, CDP-571//BAY-10-3356, cA2, 75 kdTNFR-IgG, 55 kdTNFR-IgG, Cytokine Regulating Agents (CRAs) HP228 and HP466, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, including diethylenetriamine pentaacetic acid - iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, and Synthetic Anti-Endotoxin Peptides.

97. The method of any one of claims 84, 85, 86, or 87, wherein the disorder is adult respiratory distress syndrome (ARDS).

98. The method of claim 97, wherein the additional therapeutic agent is selected from the group consisting of anti-IL-8 antibodies, surfactant replacement therapy, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG, and 55 kdTNFR-IgG.

99. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent, such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1×10^{-8} M or less and a K_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1×10^{-7} M or less.

100. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent such that the disorder is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

101. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent, such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2

102 A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, comprising administering to the subject an antibody and at least one additional therapeutic agent such that the disorder is treated, wherein the antibody is D2E7.

103. The method of any one of claims 99, 100, 101, or 102, wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, thalidomide-related drugs, leflunomide, tranexamic acid, T614,

prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered peptides, collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immune globulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, azaribine, budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, lignocaine, prednisolone, methylprednisolone, cyclophosphamide, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, hypertonic saline solutions, antibiotics, continuous hemofiltration, carbapenems, antagonists of cytokines such as TNFα, IL-1β, IL-6 and/or IL-8, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, including diethylenetriamine pentaacetic acid - iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, Synthetic Anti-Endotoxin Peptides, surfactant replacement therapy and anti-IL-8 antibodies.

104. The method of any one of claims 99, 100, 101, or 102, wherein the disorder is rheumatoid arthritis.

105. The method of claim 104, wherein the wherein the additional therapeutic agent is selected from the group consisting of non-steroidal anti-inflammatory drugs, cytokine suppressive anti-inflammatory drugs, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG , 55 kdTNFR-IgG, IDEC-CE9.1/SB 210396, DAB 486-IL-2, DAB 389-IL-2, Anti-Tac, IL-4, IL-10, IL-4 agonists, IL-10 agonists, IL-1RA, TNF-bp/s-TNFR, S284, R973401, MK-966, Iloprost, methotrexate, thalidomide, thalidomide-related drugs, leflunomide, tranexamic acid, T614, prostaglandin E1, Tenidap, Naproxen, Meloxicam, Piroxicam, Diclofenac, Indomethacin, Sulfasalazine, Azathioprine, ICE inhibitors, zap-70 inhibitors, lck inhibitors, VEGF inhibitors, VEGF-R inhibitors, corticosteroids, TNF-convertase inhibitors, anti-IL-12 antibodies, interleukin-11, interleukin-13, interleukin-17 inhibitors, gold, penicillamine, chloroquine, hydroxychloroquine, chlorambucil, cyclophosphamide, cyclosporin, anti-thymocyte globulin, anti-CD4 antibodies, CD5-toxins, orally-administered peptides, collagen, lobenzarit disodium, Cytokine Regulating Agents HP228 and HP466, ICAM-1 antisense phosphorothioate oligodeoxynucleotides, soluble complement receptor 1, prednisone, orgotein, glycosaminoglycan polysulphate, minocycline, anti-IL2R antibodies, marine lipids, botanical lipids, auranofin, phenylbutazone, meclofenamic acid, flufenamic acid, intravenous immune globulin, zileuton, mycophenolic acid, tacrolimus, sirolimus, amiprilose, cladribine, and azaribine.

106. The method of any one of claims 99, 100, 101, or 102, wherein the disorder is inflammatory bowel disease.

107. The method of claim 106, wherein the additional therapeutic agent is selected from the group consisting of budenoside, epidermal growth factor, aminosalicylates, 6-mercaptopurine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, glucuronide-conjugated prodrugs of prednisolone, dexamethasone or budesonide, dextran-conjugated prodrugs of prednisolone, dexamethasone or budesonide, soluble complement receptor 1, slow-release mesalazine, antagonists of Platelet Activating Factor (PAF), ciprofloxacin, and lignocaine.

108. The method of any one of claims 99, 100, 101, or 102, wherein the disorder is multiple sclerosis.

109. The method of claim 108, wherein the additional therapeutic agent is selected from the group consisting of corticosteroids, prednisolone, methylprednisolone, azathioprine, cyclophosphamide, cyclosporine, methotrexate, 4-aminopyridine, tizanidine, interferon-β1a, interferon-β1b, Copolymer 1, hyperbaric oxygen, intravenous immunoglobulin, clabribine, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG, 55 kdTNFR-IgG, IL-10, IL-4, and IL-10 agonists, and IL-4 agonists.

110. The method of any one of claims 99, 100, 101, or 102, wherein the disorder is sepsis.

111. The method of claim 110, wherein the additional therapeutic agent is selected from the group consisting of hypertonic saline solutions, antibiotics, intravenous gamma globulin, continuous hemofiltration, carbapenems, antagonists of TNFα, antagonists of IL-1β, antagonists of IL-6, antagonists of IL-8, CDP-571//BAY-10-3356, cA2, 75 kdTNFR-IgG, 55 kdTNFR-IgG, Cytokine Regulating Agents (CRAs) HP228 and HP466, SK&F 107647, tetravalent guanylhydrazone CNI-1493, Tissue Factor Pathway Inhibitor, PHP, iron chelators and chelates, including diethylenetriamine pentaacetic acid - iron (III) complex, lisofylline, PGG-Glucan, apolipoprotein A-1 reconstituted with lipids, chiral hydroxamic acids, anti-endotoxin antibodies, E5531, $rBPI_{21}$, and Synthetic Anti-Endotoxin Peptides.

112. The method of any one of claims 99, 100, 101, or 102, wherein the disorder is adult respiratory distress syndrome (ARDS).

113. The method of claim 112, wherein the additional therapeutic agent is selected from the group consisting of anti-IL-8 antibodies, surfactant replacement therapy, CDP-571/BAY-10-3356, cA2, 75 kdTNFR-IgG, and 55 kdTNFR-IgG.

114. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human TNFα with a K_d of 1 x 10^{-8} M or less and a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human TNFα cytotoxicity in a standard *in vitro* L929 assay with an IC_{50} of 1 x 10^{-7} M or less.

115. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1 x 10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

116. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a

light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

117. A method for inhibiting human TNFα activity in a human subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the human subject an antibody such that human TNFα activity in the human subject is inhibited, wherein the antibody is D2E7.

118. A method for treating a subject suffering from a disorder in which tnfα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen-binding portion thereof, that dissociates from human tnfα with a k_d of 1×10^{-8} m or less and a k_{off} rate constant of 1×10^{-3} s^{-1} or less, both determined by surface plasmon resonance, and neutralizes human tnfα cytotoxicity in a standard *in vitro* l929 assay with an ic_{50} of 1×10^{-7} m or less.

119. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or antigen-binding portion thereof, with the following characteristics:

a) dissociates from human TNFα with a K_{off} rate constant of 1×10^{-3} s^{-1} or less, as determined by surface plasmon resonance;

b) has a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, or modified from SEQ ID NO: 3 by a single alanine substitution at position 1, 4, 5, 7 or 8 or by one to five conservative amino acid substitutions at positions 1, 3, 4, 6, 7, 8 and/or 9;

c) has a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, or modified from SEQ ID NO: 4 by a single alanine substitution at position 2, 3, 4, 5, 6, 8, 9, 10 or 11 or by one to five conservative amino acid substitutions at positions 2, 3, 4, 5, 6, 8, 9, 10, 11 and/or 12.

120. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is an isolated human antibody, or an antigen binding portion thereof, with a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2

121. A method for treating a subject suffering from a disorder in which TNFα activity is detrimental, wherein the disorder is selected from the group consisting of periodontal disease, obesity, and radiation toxicity, comprising administering to the subject an antibody such that the disorder is treated, wherein the antibody is D2E7.